The claims defining the invention are as follows:

1. A method of identifying a subject predisposed to ischemic stroke, the method including the step of identifying a mutation in the subject that reduces the release rate of tissue plasminogen activator.

2. A method according to claim 1, wherein the ischemic stroke is a lacunar stroke.

3. A method according to claims 1 or 2, wherein the mutation is located in the tissue plasminogen activator locus.

4. A method according to claim 3, wherein the mutation is located in an upstream region of the tissue plasminogen activator locus.

5. A method according to claims 3 or 4, wherein the mutation is located in an enhancer element of the tissue plasminogen activator locus.

6. A method according to any one of claims 3 to 5, wherein the mutation is in both alleles of the tissue plasminogen activator locus.

7. A method according to claim 6, wherein the mutation is a cytosine to thymine mutation at position –7351 of the upstream region of the tissue plasminogen locus.

8. A method according to any one of claims 1 to 7, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

9. A method according to any one of claims 1 to 8, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

10. A method of identifying a subject predisposed to small vessel occlusion, the method including the step of identifying a mutation in the subject that reduces the release rate of tissue plasminogen activator.

11. A method according to claim 10, wherein the small vessel occlusion manifests clinically as a lacunar stroke, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, and vascular impotence.

12. A method according to claim 10, wherein the small vessel occlusion manifests clinically as a lacunar stroke.

13. A method according to any one of claims 10 to 12, wherein the mutation is located in the tissue plasminogen activator locus.

14. A method according to claim 13, wherein the mutation is a located in an upstream region of the tissue plasminogen activator locus.

15. A method according to claims 13 or 14, wherein the mutation is located in an enhancer element of the tissue plasminogen activator locus.

16. A method according to any one of claims 13 to 15, wherein the mutation is in both alleles of the tissue plasminogen activator locus.

17. A method according to claim 16, wherein the mutation is a cytosine to thymine mutation at position –7351 of the upstream region of the tissue plasminogen locus.

18. A method according to any one of claims 10 to 17, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

19. A method according to any one of claims 10 to 18, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

20. A method of identifying a subject predisposed to a disease or condition associated with small vessel occlusion, the method including the step of identifying a mutation in the subject that reduces the release rate of tissue plasminogen activator.

21. A method according to claim 20, wherein the disease or condition is a lacunar stroke, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, or vascular impotence.

22. A method according to claim 20, wherein the condition is a lacumar stroke.

23. A method according to any one of claims 20 to 22, wherein the mutation is located in the tissue plasminogen activator locus.

24. A method according to claim 23, wherein the mutation is a located in an upstream region of the tissue plasminogen activator locus.

25. A method according to claims 23 or 24, wherein the mutation is located in an enhancer element of the tissue plasminogen activator locus.

26. A method according to any one of claim 23 to 25, wherein the mutation is in both alleles of the tissue plasminogen activator locus.

27. A method according to claim 26, wherein the mutation is a cytosine to thymine mutation at position –7351 of the upstream region of the tissue plasminogen locus.

28. A method according to any one of claims 20 to 27, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

29. A method according to any one of claims 20 to 28, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

30. A method of identifying a subject suitable for intervention to prevent and/or treat ischemic stroke, the method including the step of identifying a mutation in the subject that reduces the release rate of tissue plasminogen activator.

31. A method according to claim 27, wherein the ischemic stroke is a lacunar stroke.

32. A method according to claims 30 or 32, wherein the mutation is located in the tissue plasminogen activator locus.

33. A method according to claim 32, wherein the mutation is located in an upstream region of the tissue plasminogen activator locus.

34. A method according to claims 32 or 33, wherein the mutation is located in an enhancer element of the tissue plasminogen activator locus.

35. A method according to claim 35, wherein the mutation is in both alleles of the tissue plasminogen activator locus.

36. A method according to claim 35, wherein the mutation is a cytosine to thymine mutation at position –7351 of the upstream region of the tissue plasminogen locus.

37. A method according to any one of claims 30 to 36, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

38. A method according to any one of claims 30 to 37, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

39. A method of identifying a subject suitable for intervention to prevent and/or treat a small vessel occlusion or a disease or condition associated with small vessel occlusion, the method including the step of identifying a mutation in the subject that reduces the release rate of tissue plasminogen activator.

40. A method according to claim 39, wherein the disease or condition is a lacunar stroke, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, or vascular impotence.

41. A method according to claim 39, wherein the condition is a lacunar stroke.

42. A method according to any one of claims 39 to 41, wherein the mutation is located in the tissue plasminogen activator locus.

43. A method according to claim 42, wherein the mutation is a located in an upstream region of the tissue plasminogen activator locus.

44. A method according to claims 42 or 43, wherein the mutation is a mutation located in an enhancer element of the tissue plasminogen activator locus.

45. A method according to any one of claims 42 to 44, wherein the mutation is in both alleles of the tissue plasminogen activator locus.

46. A method according to claim 45, wherein the mutation is a cytosine to thymine mutation at position –7351 of the upstream region of the tissue plasminogen locus.

47. A method according to any one of claims 39 to 46, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

48. A method according to any one of claims 39 to 47, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

49. A method of treating a disease or condition associated with small vessel occlusion in a subject, the method including the step of administering to the subject a therapeutically effective amount of an agent that increases the rate of release of tissue plasminogen activator in the subject.

50. A method according to claim 49, wherein the disease or condition is a lacunar stroke, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, or vascular impotence.

51. A method according to claim 49, wherein the condition is a lacunar stroke.

52. A method of treating a subject susceptible to a disease or condition associated with small vessel occlusion, the method including the step of administering to the subject a therapeutically effective amount of an agent that increases the rate of release of tissue plasminogen activator in the subject.

53. A method according to claim 52, wherein the disease or condition is a lacunar stroke, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, or vascular impotence.

54. A method according to claim 52, wherein the condition is a lacunar stroke.

55. A method of identifying an agent capable of increasing the release rate of tissue plasminogen activator from a cell, the method including the steps of:

(a) exposing an agent to a cell including a mutation that decreases the release rate of tissue plasminogen activator from the cell;

(b) determining the release rate of tissue plasminogen activator from the cell so exposed to the agent; and

(c) identifying the agent as an agent capable of increasing the release rate of tissue plasminogen activator from the cell.

56. A method according to claim 55, wherein the cell is an endothelial cell.

57. A method according to claims 55 or 56, wherein the mutation is in the tissue plasminogen activator locus.

58. A method according to claim 57, wherein the mutation is located in the upstream region of the tissue plasminogen activator locus.

59. A method according to claims 57 or 58, wherein the mutation is located in an enhancer element of the tissue plasminogen activator locus.

60. A method according to any one of claims 57 to 59, wherein the mutation is in both alleles of the tissue plasminogen activator locus.

61. A method according to claim 60, wherein the mutation is a cytosine to thymine mutation at position –7351 of the upstream region of the tissue plasminogen locus.

62. A method according to any one of claims 55 to 61, wherein the determination of the release rate of tissue plasminogen activator includes immunological detection of tissue plasminogen activator.

63. A method of identifying a subject predisposed to ischemic stroke, the method including the step of identifying in the subject the presence of a cytosine to thymine mutation at position –7351 in both alleles of the tissue plasminogen activator locus.

64. A method according to claim 63, wherein the ischemic stroke is a lacunar stroke.

65. A method according to claims 63 or 64, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

66. A method according to any one of claims 63 to 65, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

67. A method of identifying a subject predisposed to small vessel occlusion, the method including the step of identifying in the subject the presence of a

cytosine to thymine mutation at position –7351 in both alleles of the tissue plasminogen activator locus.

68. A method according to claim 67, wherein the small vessel occlusion manifests clinically as a lacunar stroke, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, and vascular impotence.

69. A method according to claim 67, wherein the small vessel occlusion manifests clinically as a lacunar stroke.

70. A method according to any one of claims 67 to 69, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

71. A method according to any one of claims 67 to 70, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

72. A method of identifying a subject predisposed to a disease or condition associated with small vessel occlusion, the method including the step of identifying in the subject the presence of a cytosine to thymine mutation at position –7351 in both alleles of the tissue plasminogen activator locus.

73. A method according to claim 72, wherein the disease or condition is a lacunar stroke, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, or vascular impotence.

74. A method according to claim 72, wherein the condition is a lacunar stroke.

75. A method according to any one of claims 72 to 74, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

76. A method according to any one of claims 72 to 75, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

77. A method of identifying a subject suitable for intervention to prevent and/or treat ischemic stroke, the method including the step of identifying in the subject the presence of a cytosine to thymine mutation at position –7351 in both alleles of the tissue plasminogen activator locus.

78. A method according to claim 77, wherein the ischemic stroke is a lacunar stroke.

79. A method according to claims 77 or 78, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

80. A method according to any one of claims 77 to 79, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

81. A method of identifying a subject suitable for intervention to prevent and/or treat a small vessel occlusion or a disease or condition associated with small vessel occlusion, the method including the step of identifying in the subject the presence of a cytosine to thymine mutation at position –7351 in both alleles of the tissue plasminogen activator locus.

82. A method according to claim 81, wherein the disease or condition is a lacunar stroke, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, or vascular impotence.

83. A method according to claim 81, wherein the condition is a lacunar stroke.

84. A method according to any one of claims 81 to 83, wherein the identification of the mutation includes amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

85. A method according to any one of claims 81 to 84, wherein the identification of the mutation includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

86. A method of identifying a subject suitable for treatment with an agent that increases the rate of release of tissue plasminogen activator, the method including the step of identifying in the subject the presence of a cytosine to thymine mutation at position –7351 in both alleles of the tissue plasminogen activator locus.

87. A method according to claim 85, wherein the subject is predisposed to, or suffering from, an ischemic stroke.

88. A method according to claim 87, wherein the ischemic stroke is a lacunar stroke.

89. A method according to claim 86, wherein the subject is predisposed to, or suffering from, a disease or condition associated with small vessel occlusion.

90. A method according to claim 84, wherein the disease or condition is dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, or vascular impotence.

91. A method of determining the risk of ischemic stroke in a subject, the method including the step of determining the presence in the subject of a cytosine to thymine mutation at position –7351 in one or both alleles of the tissue plasminogen activator locus.

92. A method according to claim 91, wherein the ischemic stroke is a lacunar stroke.

93. A method according to claims 91 or 92, wherein the determination of the presence in the subject of a cytosine to thymine mutation at position –7351 in one or both alleles of the tissue plasminogen locus includes identification of the mutation by amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

94. A method according to any one of claims 91 to 93, wherein the determination of the presence in the subject of a cytosine to thymine mutation at position –7351 in one or both alleles of the tissue plasminogen locus includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

95. A method according to any one of claims 91 to 94, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in one allele of the tissue plasminogen activator locus indicates an increased risk of ischemic stroke in the subject, as compared to the risk of ischemic stroke for a subject not having the mutation in either allele of the tissue plasminogen locus.

96. A method according to any one of claims 91 to 94, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in one allele of the tissue plasminogen activator locus indicates an increased risk of ischemic stroke in the subject, as compared to the risk of ischemic stroke for a subject in the general population.

97. A method according to any one of claims 91 to 94, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in one allele of the tissue plasminogen activator locus indicates an increased risk of ischemic stroke in the subject, as compared to the risk of schemic stroke for another subject with similar other risk factors for having an ischemic stroke.

98. A method according to any one of claims 91 to 94, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in both alleles of the tissue plasminogen activator locus indicates an increased risk of ischemic stroke in the subject, as compared to the risk of ischemic stroke for a subject not having the mutation in one or both alleles of the tissue plasminogen locus.

99. A method according to any one of claims 91 to 94, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in both alleles of the tissue plasminogen activator locus indicates an increased risk of ischemic stroke in the subject, as compared to the risk of ischemic stroke for a subject in the general population.

100. A method according to any one of claims 91 to 94, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in both allele of the tissue plasminogen activator locus indicates an increased risk of ischemic stroke in the subject, as compared to the risk of ischemic stroke for a subject with similar other risk factors for having an ischemic stroke.

101. A method of determining the risk of small vessel occlusion in a subject, or the risk of developing a disease or condition associated with small vessel occlusion in a subject, the method including the step of determining the

presence in the subject of a cytosine to thymine mutation at position –7351 in one or both alleles of the tissue plasminogen activator locus.

102. A method according to claim 101, wherein the disease or condition or condition associated with small vessel occlusion is a lacunar stroke, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, or vascular impotence.

103. A method according to claims 101 or 102, wherein the determination of the presence in the subject of a cytosine to thymine mutation at position –7351 in one or both alleles of the tissue plasminogen locus includes identification of the mutation by amplification of a region containing the mutation from nucleic acid isolated or derived from the subject.

104. A method according to any one of claims 101 to 103, wherein the determination of the presence in the subject of a cytosine to thymine mutation at position –7351 in one or both alleles of the tissue plasminogen locus includes detection of the mutation by hybridisation of nucleic acid isolated or derived from the subject to a reporter nucleic acid.

105. A method according to any one of claims 101 to 104, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in one allele of the tissue plasminogen activator locus indicates an increased risk of small vessel occlusion or developing a disease associated with small vessel occlusion in the subject, as compared to the risk for a subject not having the mutation in either alleles of the tissue plasminogen locus.

106. A method according to any one of claims 101 to 104, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in one allele of the tissue plasminogen activator locus indicates an increased risk

of small vessel occlusion or developing a disease associated with small vessel occlusion in the subject, as compared to the risk for a subject in the general population.

107. A method according to any one of claims 101 to 104, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in one allele of the tissue plasminogen activator locus indicates an increased risk of small vessel occlusion or developing a disease associated with small vessel occlusion in the subject ischemic stroke in the subject, as compared to the risk for another subject with similar other risk factors for having a small vessel occlusion.

108. A method according to any one of claims 101 to 104, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in both alleles of the tissue plasminogen activator locus indicates an increased risk of small vessel occlusion or developing a disease associated with small vessel occlusion in the subject, as compared to the risk for a subject not having the mutation in one or both alleles of the tissue plasminogen locus.

109. A method according to any one of claims 101 to 104, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in both alleles of the tissue plasminogen activator locus indicates an increased risk of small vessel occlusion or developing a disease associated with small vessel occlusion in the subject, as compared to the risk for a subject in the general population.

110. A method according to any one of claims 101 to 104, wherein the presence in the subject of a cytosine to thymine mutation at position –7351 in both allele of the tissue plasminogen activator locus indicates an increased risk of small vessel occlusion or developing a disease associated with small vessel occlusion in the subject, as compared to the risk for another subject with similar other risk factors for having a small vessel occlusion.

111. A method of identifying an agent capable of altering the release rate of tissue plasminogen activator from a cell, the method including the steps of:

(a) exposing an agent to a cell including a cytosine to thymine polymorphism at position –7351 in one or both alleles of the tissue plasminogen activator locus;

(b) determining the release rate of tissue plasminogen activator from the cell so exposed to the agent; and

(c) identifying the agent as an agent capable of altering the release rate of tissue plasminogen activator from the cell.

112. Amethod of identifying an agent capable of increasing the release rate of tissue plasminogen activator from a cell, the method including the steps of:

(a) exposing an agent to a cell transformed with all or part of the tissue plasminogen activator locus, wherein the transformed locus includes a cytosine to thymine mutation at position –7351 and the transformed locus regulates expression of a reporter gene;

(b) determining the level of expression of the reporter gene in the cell so exposed to the agent;

(c) identifying an agent capable of increasing the expression of the reporter gene; and

(d) identifying the agent capable of increasing the expression of the reporter gene as an agent capable of increasing the release rate of tissue plasminogen activator from a cell.

113. An isolated nucleic acid consisting of the sequence according to SEQ. ID No.3 or RNA equivalent thereof.

114. An isolated nucleic acid with one or more base substitutions in the sequence according to SEQ ID No. 3, wherein the nucleic acid hybridises with the complement of SEQ ID No.3 under stringent hybridisation conditions and the stringent hybridisation conditions include hybridisation in 6xSSC at 42°C and washing in 2xSSC at 20°C.

115. An isolated nucleic acid consisting of the sequence according to SEQ. ID No.4 or RNA equivalent thereof.

116. An isolated nucleic acid with one or more base substitutions in the sequence according to SEQ ID No. 4, wherein the nucleic acid hybridises with the complement of SEQ ID No. 4 under stringent hybridisation conditions and the stringent hybridisation conditions include hybridisation in 6xSSC at 42°C and washing in 2xSSC at 20°C.

117. An isolated nucleic acid with one or more base substitutions in the sequence according to SEQ ID No. 3, wherein the nucleic acid has at least 80% homology to SEQ. ID No.3 or RNA equivalent thereof.

118. An isolated nucleic acid with one or more base substitutions in the sequence according to SEQ ID No. 4, wherein the nucleic acid has at least 80% homology to SEQ. ID No.4 or RNA equivalent thereof.

119. An isolated nucleic acid, the nucleic acid consisting of the sequence spanning nucleotides 1840 to 2245 of SEQ ID No. 1.

120. A method of identifying a subject predisposed to ischemic stroke, the method include the step of identifying a reduced rate of release of tissue plasminogen activator in the subject.

121. A method according to claim 120, wherein the ischemic stroke is a lacunar stroke.

122. A method of identifying a subject predisposed to a small vessel occlusion, the method including the step of identifying a reduced rate of release of tissue plasminogen activator in the subject.

123. A method according to claim 122, wherein the small vessel occlusion manifests clinically as a lacunar stroke, dementia, ischemic heart disease

(including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, and vascular impotence.

124. A method of identifying a subject predisposed to a disease or condition associated with small vessel occlusion, the method including the step of identifying a reduced release rate of tissue plasminogen activator in the subject.

125. A method according to claim 124, wherein the disease or condition is a lacunar stroke, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, and vascular impotence.

126. A method of identifying a subject suitable for intervention to prevent and/or treat ischemic stroke, the method including the step of identifying a reduced release rate of tissue plasminogen activator in the subject.

127. A method according to claim 126, wherein the ischemis stroke is a lacunar stroke.

128. A method of identifying a subject suitable for intervention to prevent and/or treat a small vessel occlusion or a disease or condition associated with small vessel occlusion, the method including the step of identifying a reduced release rate of tissue plasminogen activator in the subject.

129. A method according to claim 128, wherein the disease or condition associated with small vessel occlusion is a lacunar stroke, dementia, ischemic heart disease (including ischemic cardiomyopathy), peripheral vascular disease, disseminated intravascular coagulation, small vessel vasculitis, ischemic

neuropathy, ischemic retinopathy, ischemic gastropathy (including small and large bowel ischemia), diffuse pulmonary embolism, and vascular impotence.

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